

## CLAIM AMENDMENTS

1. (currently amended) A modified nucleotide compound which includes at least one component selected from the group consisting of  $MN_3M$ ,  $(N)_xM(N)_y$ ,  $(N)_xM(N)_yM$ ,  $B(N)_xM(N)_y$  and  $(N)_xM(N)_yB$  wherein:

N is a phosphodiester-linked modified or unmodified 2'-deoxynucleoside moiety; provided that at least one N is a phosphodiester-linked unmodified 2' deoxynucleoside moiety;

M is a moiety that confers endonuclease resistance on said component and that contains at least one modified or unmodified nucleic acid base;

B is a moiety that confers exonuclease resistance to the terminus to which it is attached;

x is an integer of at least 2; and

y is an integer.

wherein the compound acts as an RNase H substrate when complexed with a complementary RNA

2. (original) The modified nucleotide compound of claim 1 wherein M and B are the same moiety.

Claim 3 (cancelled)

4. (original) The modified nucleotide compound of claim 1 wherein N contains at least one adenine, guanine, thymine or cytosine moiety.

5. (original) The modified nucleotide compound of claim 1 wherein N contains at least one uracil, inosine or 2, 6-diaminopurine moiety.
6. (original) The modified nucleotide compound of claim 1 wherein N contains at least one 5-halogenated uracil or cytosine or a substituted or unsubstituted 7-deazaguanine, 7-deazaadenine or 7-deazainosine moiety.
7. (original) The modified nucleotide compound of claim 1 wherein N contains at least one methylated adenine, guanine, thymine or cytosine moiety.
8. (original) The modified nucleotide compound of claim 1 wherein M is a  $C_1 - C_4$  alkylphosphonate deoxynucleotide.
9. (original) The modified nucleotide compound of claim 8 wherein M is a methylphosphonate deoxynucleotide.
10. (original) The modified nucleotide compound of claim 1 wherein M is an alpha-phosphodiester 2'deoxy nucleoside.
11. (currently amended) The modified nucleotide compound of claim 1 wherein M is selected from the group consisting of an aminophosphonate, phosphotriester, phosphoramidate, carbamate or morpholino-substituted nucleotide.
12. (original) The modified nucleotide compound of claim 1 wherein B is directly or indirectly attached to the deoxyribose moiety of at least one of the 3'-and 5'- terminal nucleotides.

13. (original) The modified nucleotide compound of claim 12 wherein B is directly or indirectly attached to a hydroxyl group of the deoxyribose of at least one of the 3'-and 5'- terminal nucleotides.

14. (original) The modified nucleotide compound of claim 12 wherein B is directly or indirectly attached to a phosphate moiety attached to the deoxyribose moiety of at least one of the 3'- and 5'- terminal nucleotides.

15. (original) The modified nucleotide compound of claims 13 or 14 wherein B is selected from the group consisting of an intercalating agent, an isourea a carbodiimide and an N-hydroxybenzotriazole.

16. (original) The modified nucleotide compound of claim 13 wherein B is a methylthiophosphonate.

17. (original) The modified nucleotide compound of claims 13 or 14 wherein B is a polypeptide or protein.

18. (original) A modified nucleotide compound of claim 1 which includes at least one sequence of the formula  $(N)_y M(N)_x B$  wherein B is a modified or unmodified 2', 3'-dideoxyribose nucleotide.

19. (original) The modified nucleotide compound of claim 1 wherein y is an integer selected from the group consisting of 2 or 3.

20. (currently amended) A modified nucleotide compound which contains at least one sequence having the formula  $MN_3M$  wherein N is a phosphodiester-linked unmodified 2'-deoxynucleoside moiety containing at least one guanine, adenine, cytosine or thymine moiety and M is a methylphosphonate-containing deoxynucleotide, wherein the compound acts as an RNase H substrate when complexed with a complementary RNA.

21. (currently amended) A method of inhibiting the function of an RNA, which comprises: contacting said RNA, under conditions permissive of hybridization, with a modified nucleotide compound which acts as an RNase H substrate when complexed with a complementary RNA which includes at least one complimentary component selected from the group consisting of  $MN_3M$ ,  $(N)_xM(N)_y$ ,  $(N)_xM(N)_yM$ ,  $B(N)_xM(N)_y$  and  $(N)_xM(N)_yB$  wherein:

N is a phosphodiester-linked modified or unmodified 2'-deoxynucleoside moiety;

M is a moiety whose presence confers endonuclease resistance on said component and that contains at least one modified or unmodified nucleic acid base;

B is a moiety whose presence confers exonuclease resistance to the terminus to which it is attached; and

x is an integer of at least 2.

22. (original) The method of claim 21 wherein the RNA is contacted with a compound wherein M and B are the same moiety.

23. (original) The method of claim 21 wherein the RNA is contacted with a compound wherein N contains at least one adenine, guanine, thymine or cytosine moiety.

24. (original) The method of claim 21 wherein the RNA is contacted with a compound wherein N contains at least one uracil, inosine or 2, 6-diaminopurine moiety.

25. (original) The method of claim 21 wherein the RNA is contacted with a compound wherein N contains at least one 5-halogenated uracil or cytosine or a substituted or unsubstituted 7-deazaguanine, 7-deazaadenine or 7-deazainosine moiety.

26. (original) The method of claim 21 wherein the RNA is contacted with a compound wherein N contains at least one methylated adenine, guanine, thymine or cytosine moiety.

27. (original) The method of claim 21 wherein the RNA is contacted with a compound wherein M is a C<sub>1</sub>-C<sub>4</sub> alkylphosphonate.

28. (original) The method of claim 27 wherein the RNA is contacted with a compound wherein M is a methylphosphonate.

29. (original) The method of claim 21 wherein the RNA is contacted with a compound wherein M is an alpha-phosphodiester 2'deoxy nucleoside.

30. (original) The method of claim 21 wherein the RNA is contacted with a compound wherein M is selected from the group consisting of an aminophosphonate, phosphotriester, phosphoramidate, carbamate or morpholino-substituted nucleotide.

31. (original) The method of claim 21 wherein the RNA is contacted with a compound wherein B is directly or indirectly attached to the deoxyribose moiety of at least one of the 3'-and 5'- terminal nucleotides.

32. (original) The method of claim 31 wherein the RNA is contacted with a compound wherein B is directly or indirectly attached to a hydroxyl group of the deoxyribose of at least one of the 3'- and 5' terminal nucleotides.

33. (original) The method of claim 31 wherein the RNA is contacted with a compound wherein B is directly or indirectly attached to a phosphate group attached to the deoxyribose moiety of at least one of the 3'-and 5'- terminal nucleotides.

34. (original) The method of claims 32 or 33 wherein the RNA is contacted with a compound wherein B is selected from the group consisting of an intercalating agent, an isourea, a carbodiimide and an N-hydroxybenzotriazole.

35. (original) The method of claim 32 wherein the RNA is contacted with a compound wherein B is a methylthiophosphonate.

36. (original) The method of claims 32 or 33 wherein the RNA is contacted with a compound wherein B is a polypeptide or protein.

37. (original) The method of claim 21 wherein the RNA is contacted with a compound which includes at least one sequence of the formula  $(N)_y M(N)_x B$  wherein B is modified or unmodified 2', 3'-dideoxyribose nucleotide.

38. (original) The method of claim 21 wherein the RNA is contacted with a compound wherein x is selected from the group consisting of 2 or 3.

39. (original) The method of claim 21 wherein the RNA is contacted with a modified nucleotide compound which includes at least one sequence having the formula  $MN_3M$  wherein N is a phosphodiester-linked unmodified 2'-deoxynucleoside moiety containing at least one guanine, adenine, cytosine or thymine moiety and M is a methylphosphonate-containing deoxynucleoside.

40. (currently amended) A method of identifying a nucleotide compound having a combination of nuclease resistance and the ability to form an RNase H substrate when in complex with an RNA, which method comprises:

(i) preparing modified nucleotide compounds which includes at least one component selected from the group consisting of  $MN_3M$ ,  $B(N)_xM$  and  $M(N)_xB$  wherein:

N is a phosphodiester-linked modified or unmodified 2'-deoxynucleoside moiety;

M is a moiety that confers endonuclease resistance on said component and that contains at least one modified or unmodified nucleic acid base;

B is a moiety that confers exonuclease resistance to the terminus to which it is attached;

x is an integer of at least 2.

(ii) ;

~~(ii)~~(ii) selecting by exo- and endonuclease digestion those modified nucleotide compounds of (i) which are nuclease-resistant as shown by being capable of forming and electrophoretically migrating as a duplex with a complementary nucleotide compound; and

~~(iii)~~(iii) selecting by RNase H digestion those of the nuclease-resistance nucleotide compounds of (ii) which act as substrates for RNase H when hybridized with a complementary RNA.

41. (currently amended) A method of treating a human or animal so as to inhibit the function of a target RNA therein which method comprises administering a therapeutically effective amount of a modified nucleotide compound so as to inhibit the function of the target RNA, wherein said modified nucleotide compound includes at least one component selected from the group consisting of  $MN_3M$ ,  $(N)_xM(N)_y$ ,  $(N)_xM(N)_yM$ ,  $B(N)_xM(N)_y$  and  $(N)_xM(N)_yB$ ; wherein N is a phosphodiester-linked modified or unmodified 2'-deoxynucleoside moiety, M is a moiety that confers endonuclease resistance on said component and that contains at least one modified or unmodified nucleic acid base, B is a moiety that confers exonuclease resistance to the terminus to which it is attached, x is an integer of at least 2, and y is an integer and wherein said modified nucleotide compound acts as an RNase substrate when complexed with a complementary RNA.

42. (currently amended) A compound containing at least 2 separate nuclease resistant components each consisting of 2 or more contiguous phosphodiester-linked 2' deoxynucleosides; wherein at least one of said contiguous phosphodiester-linked 2' deoxynucleosides is unmodified, wherein the compound acts as an RNase H substrate when complexed with a complementary RNA and wherein each nuclease resistant component comprises at least one moiety which confers endonuclease



resistance and at least one moiety which confers exonuclease resistance and wherein said 2 or more contiguous phosphodiester-linked 2' deoxynucleosides are located between the moiety conferring endonuclease resistance and the moiety conferring exonuclease resistance.

43. (original) The compound of claim 42 which is capable of specifically binding with a nucleic acid sequence of interest to inhibit the function thereof.

Claim 44 (cancelled)

45. (original) The compound of claim 42 which comprises an oligonucleotide or polynucleotide.

46. (original) The compound of claim 45 wherein the oligonucleotide or polynucleotide is modified.

47. (original) The compound of claim 46 wherein the modified oligonucleotide or polynucleotide consists of at least one moiety which confers endonuclease resistance and at least one moiety which confers exonuclease resistance.

48. (original) The compound of claim 47 wherein the endonuclease-resistance conferring moiety also confers exonuclease resistance to the modified nucleotide component.

49. (original) The compound of claim 47 wherein the portion of the compound that can function as an RNase H substrate is located between the moiety conferring exonuclease resistance and the moiety conferring endonuclease resistance.

50. (currently amended) A compound containing at least two separate nuclease resistant sequences which consists of 2 or 3 contiguous phosphodiester-linked 2'-deoxynucleosides; wherein at least one of said contiguous phosphodiester-linked 2'-deoxynucleosides is unmodified, wherein said compound acts as an RNase H substrate when complexed with complementary RNA and wherein each nuclease resistant sequences comprise 2 or 3 contiguous phosphodiester-linked 2'-deoxynucleosides between the B and M moiety.

51. (previously amended) A modified nucleotide compound which comprises at least one component selected from the group consisting of  $MN_3M$ ,  $(N)_x M(N)_y$ ,  $(N)_x M(N)_y M$ ,  $B(N)_x M(N)_y$  and  $(N)_x M(N)_y B$  wherein:

N comprises a phosphodiester-linked modified 2' deoxynucleoside moiety;

M is a moiety that confers endonuclease resistance on said component and which contains at least one nucleic acid base with a 3' methoxylphosphonate;

B is a moiety that confers exonuclease resistance to the terminus to which it is attached and comprises a 2', 3'-dideoxyribose nucleotide;

x is an integer of about 2; and

y is an integer.

52. (previously presented) A modified nucleotide compound capable of forming RNase H sensitive hybrids and having improved nuclease resistance comprising at least one non-terminal moiety that confers nuclease resistance on said compound and contains at least one modified or unmodified nucleic acid base and at least one non-terminal phosphodiester-linked unmodified 2' deoxynucleoside moiety.
53. (new) The modified nucleotide compound of claim 1, wherein M is a phosphotriester.
54. (new) A modified nucleotide compound which includes at least one component selected from the group consisting of  $MN_3$  M,  $B(N)_x$  M and  $(N)_x M(N)_y B$  wherein:
- N is a phosphodiester-linked modified or unmodified 2'-deoxynucleoside moiety; provided that at least one N is a phosphodiester-linked unmodified 2' deoxynucleoside moiety;
  - M is a moiety that confers endonuclease resistance on said component and that contains at least one modified or unmodified nucleic acid base;
  - B is a moiety that confers exonuclease resistance to the terminus to which it is attached;
  - x is an integer of at least 2
- wherein said compound acts as an RNase H substrate when complexed with complementary RNA and wherein when the compound is  $B(N)_x$  M or  $(N)_x M(N)_y B$ , M is selected from the group consisting of an alkylphosphonate, aminophosphonate, phosphotriester, phosphoramidate, carbamate and morpholino-substituted nucleotide.